I. Scientific Abstract

This is a phase I trial to evaluate DNA vaccination in patients with metastatic melanoma. The objective of this study is to determine the safety and immunogenicity of vaccination with the genes coding for mouse and human tyrosinase in patients with AJCC stage III and IV melanoma who are HLA-A2+. We will assess whether DNA vaccination is safe and generates an immune response to an otherwise poorly immunogenic melanoma differentiation antigen.

The hypothesis that xenogeneic DNA encoding a homologous antigen is more potent than syngeneic DNA encoding a tumor antigen will be tested. A randomized crossover design of a phase I study will be used to assess this hypothesis. We will assess two closely related DNA vaccines against tyrosinase. Studies in animal models have demonstrated that xenogeneic DNA (i.e., homologous DNA from a different species) can be more potent in inducing antibody and T cell responses against melanoma differentiation antigens than vaccination with self DNA. Patients will be randomly assigned to vaccination with either xenogeneic (mouse) or human tyrosinase DNA delivered both intradermally and intramuscularly at three different dose levels (100, 500, or 1500 μg in divided doses) every three weeks for three immunizations. Following this initial vaccination period, those patients previously randomized to receive mouse tyrosinase DNA will receive three immunizations with human tyrosinase DNA at three week intervals. Likewise, those patients initially randomized to receive human tyrosinase DNA will then receive three immunizations with mouse tyrosinase DNA at three week intervals. If patients have stable or clinically responding disease, additional vaccinations are administered bimonthly for up to four additional vaccinations. A total of at least 18 patients are planned. Patients' sera and peripheral blood mononuclear cells will be collected in order to measure the antibody and T cell responses induced by the vaccines. Specifically, titers of IgM and IgG antibodies against human and mouse tyrosinase will be measured for serological response and Elispot assays for CD8+ T cells responses will be assessed.